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EXAMINER	
GODDARD, LAURA B	
ART UNIT	PAPER NUMBER
1642	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,759	ZHOU, MINGDONG	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6,9-14,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6,9-14,44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 March 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed March 2, 2009 in response to the Office Action of November 28, 2008, is acknowledged and has been entered. Claims 4, 6, 9-14, 44, and 45 are pending. Claims 44 and 45 are new. Previously pending claims 4, 6, and 9-14 have been amended. Claims 4, 6, 9-14, 44, and 45 are currently being examined as drawn to the elected species of protein or peptide "amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14" and species of neoplasm "breast cancer."

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NOTE: Claims 4, 44, and 45 are added to the maintained rejection below as necessitated by amendments. Issues remain the same with regards to "functional fragment thereof."

2. **Claims 6 and 6-14 remain rejected and claims 4, 44, and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection (see section 3 of the previous Office Action).

The claims are now drawn to a method for preventing, treating or delaying neoplasm in a mammal, which method comprises administering to a mammal, to which such prevention, treatment or delay is needed or desirable, an effective amount of an ErbB-3 protein, **or a functional fragment thereof**, whereby an immune response is generated against said neoplasm is prevented, treated or delayed, wherein the ErbB-3 protein comprises: (b) at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14.

Claim 4 recites that the ErbB-3 protein comprises (b) at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, however, **the claim fails to recite any structure comprised by the functional fragment thereof.**

The specification discloses that any suitable ErbB-3 protein or functional fragment thereof that can elicit an immune response to the neoplasm can be used in the present method. The specification discloses that ErbB-3 proteins or fragments disclosed in US Patent 5,820,859 can be used, or those derived from rat ErbB-3, from puffer fish ErbB-3, or derived from human ErbB-3 (p. 12, section B). The specification discloses that SEQ ID NO:14 is the ErbB-3 extracellular domain of ErbB-3 (p. 25) and the protein, SEQ ID NO:14, also named rhErbB3-f12, was used to inoculate mice. It appears rhErbB3-f12 delayed tumor growth or reduced tumor growth in inoculated mice compared to controls, however the type of cancer the mice developed is unclear (i.e.,

breast, lung, etc) (Table 4, p. 30). The specification does not disclose any other ErbB-3 functional fragments thereof as broadly encompassed in the claims.

The art (see US Patent 5,183,884, Kraus et al) teaches the sequence of human ErbB-3, and Lee et al (Cancer Research, 2001, 61:4467-4473) teach the extracellular domain of ErbB-3 that is amino acids 1-620 (Figure 1), however these sequences do not provide an adequate representative number of species to support adequate written description for the broad genus of ErbB-3 functional fragments thereof as encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a recitation of "an ErbB-3 protein, or functional fragment thereof". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The

court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-

Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of ErbB-3 functional fragments thereof, per Lilly by structurally describing representative ErbB-3 functional fragments thereof or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe ErbB-3 functional fragments thereof useful in the claimed invention in a manner that satisfies either the

Lilly or Enzo standards. Although the specification discloses human, rat, and puffer fish ErbB-3 proteins as well as extracellular domain fragment SEQ ID NO:14, this does not provide a description of the broadly claimed ErbB-3 functional fragments thereof that would satisfy the standard set out in Enzo because the specification provides no structural features coupled to functional characteristics.

Further, the specification also fails to describe ErbB-3 proteins functional fragments by the test set out in Lilly because the specification describes only human, rat, and puffer fish ErbB-3 proteins as well as extracellular domain fragment SEQ ID NO:14. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of ErbB-3 functional fragments that is required to practice the claimed invention. Since the specification fails to adequately describe the product to which the claimed method uses, it also fails to adequately describe the method.

Response to Arguments

3. Applicants argue that they amended claims to depend from claim 4 which was not originally rejected (p. 9).

The argument has been considered but is not found persuasive because claim 4 was amended only to provide written description for an erbB-3 protein and not the functional fragment thereof, for the reasons set forth above. The claim as amended recites that an erbB-3 protein comprises: (b) at least amino acid residues 24-81 of the

amino acid sequence set forth in SEQ ID NO:14, however the claim recites nothing about the structure or sequence comprised by the genus of functional fragments claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. **Claims 1, 4, 6, and 9-14 remain rejected and new claims 44 and 45 are rejected under 35 U.S.C. 102(b)** as being anticipated by WO 98/02540, Fizpatrick et al, published 1/22/1998 (see section 4 of the previous Office Action).

The claims are drawn to a method for preventing, treating or delaying neoplasm in a mammal, which method comprises administering to a mammal, to which such prevention, treatment or delay is needed or desirable, an effective amount of an ErbB-3 protein, or a functional fragment thereof, whereby an immune response is generated against said neoplasm is prevented, treated or delayed, wherein the ErbB-3 protein comprises: (b) at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14 (claim 4), the method of claim 4, further comprising administering an immune response potentiator to the mammal (claim 6), the method of claim 4, wherein the ErbB-3 protein, or the functional fragment thereof, is co-administered with a pharmaceutically acceptable carrier or excipient (claim 9), the method of claim 4,

wherein the ErbB-3 protein, or the functional fragment thereof, is co-administered with an anti-neoplasm agent (claim 10), the method of claim 10, wherein the anti-neoplasm agent is selected from the group consisting of an anti-angiogenic agent, an alkylating agent, an antimetabolite, a natural product, a platinum coordination complex, an anthracenedione, a substituted urea, a methylhydrazine derivative, an adrenocortical suppressant, a hormone, an antagonist, an oncogene inhibitor, a tumor suppressor gene or protein, an anti-oncogene antibody and an anti-oncogene antisense oligonucleotide (claim 11), the method of claim 4, wherein the neoplasm to be prevented, treated or delayed is breast cancer (claim 12-14), the method of claim 4, wherein the mammal is a human (claim 44), the method of claim 4, wherein the administering is by intracavernous injection, subcutaneous injection, intravenous injection, intramuscular injection, intradermal injection, oral administration or topical administration (claim 45).

Fizpatrick et al teach a method for treating or preventing a neoplasm in a mammal comprising administering to the mammal, the extracellular domain protein of human ErbB-3 (p. 8, line 38 through p. 9, line 12; p. 9, lines 32 through p. 10, line 3; p. 19, lines 31-33; p. 27, lines 8-9; Examples 2-3; claims 7, 37, 38), wherein the neoplasm is breast cancer (p. 15, line 10; p. 25, lines 1-10), wherein the mammal is human (p. 19, lines 34-36), wherein the ErbB-3 protein is administered in a pharmaceutically acceptable carrier or excipient (p. 19, lines 37 to p. 20, line 2; p. 26, lines 3-14), wherein the ErbB-3 protein is administered with an immune response potentiator or adjuvant such as a cytokine (p. 27, lines 19-20), wherein the ErbB-3 protein is co-administered

with an antineoplastic agent which includes anti-angiogenic agents and antibody antagonists of oncogene growth receptors (p. 27, 10-20), wherein the ErbB-3 protein is administered by intravenous, intraperitoneal, intraarterial injection (p. 26, lines 22-25), and wherein the ErbB-3 protein comprises the N-terminal 636 amino acids (p. 35, line 25), which includes the extracellular domain hence, necessarily comprises at least amino acid residues 24-81 of SEQ ID NO:14 of the instant application (residues 24-81 are the equivalent of residues 483-540 of ErbB-3). Given Fizpatrick et al teach a method for treating or preventing a neoplasm in a mammal comprising the same claimed step of administering to the mammal the extracellular domain protein of human ErbB-3, the method taught by Fizpatrick et al would generate an immune response against said neoplasm.

Response to Arguments

5. Applicants argue that Fizpatrick *et al.* does not teach administering to a mammal an ErbB-3 protein or a fragment thereof, wherein the ErbB-3 protein comprises (b) at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO: 14. Applicants argue that Fizpatrick *et al.* discloses chimeric heteromultimer adhesins that comprise extracellular binding domains of a natural heteromultimer receptor, and bind to the ligand of the natural receptor (see Fizpatrick *et al.,* page 1, lines 3-5). Applicants argue that Fizpatrick *et al.* discloses chimeric heteromultimer adhesins that comprises extracellular domains of a pair of monomers of the natural receptor ErbB2/ErbB3 and ErbB2/ErbB4 (see Fizpatrick *et al.,* page 8, lines 8-11). Applicants argue that Fizpatrick *et al* further discloses that the chimeric heteromultimer adhesins can either be a

chimeric heterodimer immunoadhesin, such as ErbB2/3-IgG, ErbB2/4-IgG, or ErbB3/4-IgG, or a chimeric homodimer immunoadhesin, such as ErbB2/2-IgG, ErbB3/3-IgG, or ErbB4/4-IgG (see Fizpatrick *et al.,* Figure 1). Applicants argue that Fizpatrick *et al.* does not teach that the chimeric heteromultimer adhesins can be only a monomer of an ErbB *(i.e.,* an ErbB-3 protein or a functional fragment thereof), much less an ErbB-3 protein (or functional fragment thereof) comprising (b) at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14 as recited in amended claim 4. Applicants point to *Verdegaal Bros. v. Union Oil Co. of California* and argue that "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Applicants argue that the method taught by Fizpatrick *et al.* does not generate the immune response recited in amended claim 4, since the chimeric heteromultimer adhesins administered by Fizpatrick *et al.* is structurally and functionally different from the ErbB-3 protein (or functional fragment thereof) used in the claimed method (p. 10).

6. The arguments have been considered but are not found persuasive because Applicants are arguing limitations not recited in the claims. Applicants admit that Fizpatrick et al teach chimeric heteromultimer adhesins that comprises extracellular domains of a pair of monomers of the natural receptor ErbB2/ErbB3 but argue that Fizpatrick et al does not teach a monomer of ErbB3 protein, however, the claims are not limited to monomers of ErbB-3 proteins. The claims broadly encompass administering to a mammal any ErbB-3 protein, or any functional fragment thereof, wherein the ErbB-

3 protein comprises (b) at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14." The adhesin taught by Fizpatrick et al comprises the extracellular domain of ErbB-3 protein which comprises the N-terminal 636 amino acids, hence, necessarily comprises at least amino acid residues 24-81 of SEQ ID NO:14 of the instant application. The method taught by Fizpatrick et al comprises administering to a mammal an erbB-3 protein or functional fragment thereof comprising at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14 as required by the claims. Further, because Fizpatrick et al teach a method comprising the identical method step as claimed, the method of Fizpatrick et al would necessarily generate an immune response, treat, prevent, or delay a neoplasm. It is noted that the "whereby" clause of claim 4 states the intended result of the step of administering to a mammal an effective amount of an ErbB-3 protein, or a functional fragment thereof, wherein the ErbB-3 protein comprises: (b) at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14. The whereby clause does not require steps to be performed and does not limit the claim to a particular structure, therefore is not given weight. See MPEP 2111.04.

7. All other rejections recited in the Office Action mailed November 28, 2008 are hereby withdrawn in view of amendments.

8. **Conclusion:** No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642